FOOD AND DRUG ADMINISTRATION (FDA)
Center for Drug Evaluation and Research (CDER)
Gastrointestinal Drugs Advisory Committee (GIDAC)
November 4, 2010
Hilton Washington DC/North, Gaithersburg, MD

Draft Questions to the Committee

1. Are endoscopically diagnosed GU/DU (gastric ulcer/duodenal ulcer) an adequate primary efficacy endpoint for evaluating products intended to prevent NSAID-associated UGI (upper gastrointestinal) toxicity (e.g. misoprostol, histamine type 2 receptor antagonists, proton pump inhibitors (PPI), and novel agents)?

2. Given that:
   - Endoscopy trials of misoprostol and PPIs in patients at risk of NSAID-associated UGI toxicity have demonstrated a relative decrease in risk of endoscopically diagnosed ulcers compared to control (RR between 0.2 to 0.4) and a 10 to 40% risk difference.

   - In an endoscopy trial that evaluated efficacy of PPI (esomeprazole), in patients receiving low dose aspirin (81 to 325 mg daily) as prophylaxis for cardiovascular protection, the risk difference was 3%; however, the relative risk was 0.3.

   How should a clinically meaningful difference be defined? Please address the type of analysis and magnitude of difference in your answer.

3. For the products discussed in Question 1, discuss the appropriate length of endoscopy trials.

4. If endoscopically-diagnosed ulcers are not adequate primary efficacy endpoints for products discussed in Question 1, then discuss why and recommend an appropriate study design.

5. Are endoscopically-diagnosed GU/DU an adequate endpoint for evaluating NSAID-associated UGI toxicity in NSAID product development (e.g. NSAID product or other novel product)?

6. If you think that endoscopically-diagnosed upper GI ulcers is an acceptable endpoint, can a clinically meaningful difference be defined a priori? Please address the type of analysis and magnitude of difference in your answer.

7. For the products discussed in Question 5, discuss the appropriate length of endoscopy trials.

8. If endoscopically diagnosed ulcers are not adequate primary efficacy endpoints for products discussed in Question 5, then discuss why and recommend an appropriate study design.

9. If endoscopically-diagnosed ulcer is not an adequate primary endpoint for either the products discussed in Question 1 and Question 5, please discuss the type of evidence that is needed to establish this endpoint for use in future registration trials.